Malnutrition and mortality

Jan Van den Broeck MD PhD DTM&H

J R Soc Med 1995;**88**:487–490

Keywords: *protein-energy malnutrition; child mortality*

INTRODUCTION

Deficient intake of energy, protein or micronutrients is a major health problem both in less developed as well as in industrialized countries. In poor areas protein-energy malnutrition (PEM) is most prevalent among preschool children, whereas in more developed areas it is most prevalent among elderly people and hospitalized patients. In any of these patient groups, epidemiologic studies have shown that the condition is associated with an increased mortality[1,2]. Mortality is the most severe complication of malnutrition.

VITAL FUNCTIONS

In malnutrition, as in any disorder, survival depends upon maintenance of vital functions. Table 1 gives a list of vital functions that can be endangered in malnutrition, the mechanisms by which this is supposed to occur and the epidemiologic correlates that are expected to result. These vital functions interact in many ways.

Vital organ fuelling in malnourished subjects depends on an increase of gluconeogenesis and the use of ketones as sources of energy[3]. This implies a negative nitrogen balance and a depletion of muscle protein and of fat reserves. If infection is associated with malnutrition, the production of ketones is impaired and protein reserves are even more depleted by gluconeogenesis and by the production of acute phase proteins and proteins involved in immunologic response and tissue repair[3]. It would be predicted, therefore, that mortality would increase in patients with severe muscle wasting, especially in the presence of infection. Mid-upper arm circumference is closely related to muscle status. Among anthropometric indicators of nutritional status this has been shown to be the best predictor of short-term mortality in children[4]. According to the muscle mass hypothesis of Briend and co-workers[5], mortality is directly related to the ratio of body muscle mass to the mass of energy requiring organs, principally the brain. This would explain that the younger the patient, the higher the risk.

Tissue oxygenation may be impaired in malnutrition for several reasons. For example, anaemia is seen very frequently in malnutrition and has often a nutritional aetiological component. Severe anaemia is known to be a frequent cause of death in children in the tropics and a bad prognostic sign in malnutrition[6,7,8]. In Mexico, Gomez and co-workers[1] identified severe bronchopneumonia as a frequent direct cause of death in hospitalized malnourished children.

Water and electrolyte balance is often impaired, especially in the most acute forms of malnutrition such as kwashiorkor. Rapid ionic shifts may occur and life threatening cardiac arrythmias may result[8]. Gomez and co-workers also found that water and electrolyte disturbances very immediately preceed death in their patients[1]. Anaemia and oedema may result in heart failure.

Body temperature maintenance: Malnourished subjects are unable to maintain their core temperature in a cold environment[7]. This may pose problems even in tropical areas, as temperatures may fall considerably at night. Hypothermia is considered to have a bad prognosis in malnutrition.

Clearance of cellular debris, free radicals and toxins (mycotoxins, gut-derived toxins, endotoxins) is another vital function. In malnutrition, hepatomegaly is considered to be the result of an excess of such products[9]. This may help to explain why mortality was found to be increased in the presence of hepatomegaly[10]. Fibronectin is a protein that plays a role in this clearance process[11]. Low serum concentrations of fibronectin correlate with poor survival and fibronectin treatment was reported significantly to improve survival both in kwashiorkor and in marasmus. The anti-oxidative properties of vitamin A are believed to be responsible for reduced mortality and reduced severity of illness observed in some vitamin A supplementation trials, even in areas without clinical signs of vitamin A deficiency[12].

Immunologic defence is impaired in malnutrition, especially T-cell function. Infections tend to last longer and lead more frequently to septicaemia. Moreover, clinical signs of infection such as fever are often absent or reduced in severe malnutrition[7]. Anorexia may be the only sign of infection. Consequently, infections are often underdiagnosed or only recognized in an advanced stage. Treatment is often delayed and becomes more difficult. This is all worse in poor areas. Poor accessability to health care[13], lack of maternal education[14], preferential concern for the health of male children[15], contribute to late, inadequate and unsustained

Bureau Nederlandse Groeistichting, Academisch Ziekenhuis Leiden, Rijnburgerweg 10, PO Box 9600, 2300 RC Leiden, The Netherlands

Table 1. **Vital functions endangered in malnutrition and epidemiologic correlates**

Vital function	(Potential) Disturbance in malnutrition	Epidemiologic correlate: mortality increased in malnutrition with
1 Vital organ fuelling	Necessity of muscle breakdown and fat depletion	Severe muscle wasting Low arm circumference
		Hypoglycaemia
2 Tissue oxygenation	Anaemia	Anaemia
	Cardiac disturbances	Concomitant cardio-pulmonary disorder
3 Water/electrolyte balance	Potassium depletion	Kwashiorkor>marasmus
	Water and sodium retention	Oedema
	Oedema (kwashiorkor)	
4 Body temperature maintenance	Deficient thermoregulation	Hypothermia
5 Clearance of debris, free radicals, toxins	Low fibronectin	Hepatomegaly
	Vitamin A deficiency	Low fibronectin
	Deficient clearance systems?	
6 Immune defence	Immunodeficiency	Infections

response to both malnutrition and infection and eventually to increased mortality, especially in girls. From the above it is clear that many factors determine the severity and prognosis of malnutrition. Metabolic exhaustion, acuteness of PEM and defence against infections are among the most important ones[16].

WEIGHT-FOR-AGE LEVELS

In clinical practice as well as in epidemiologic field studies, the severity (degree) of PEM is often assessed by different levels of weight-for-age (WFA)[1], weight-for-height (WFH)[17] or weight loss. In PEM, changes in body weight reflect combinations of different degrees of (pre)oedema, water and sodium retention, dehydration by diarrhoea, muscle wasting, depletion of glycogen and fat reserves, reduced brain weight, growth arrest, bone demineralization, hepatomegaly and atrophy of lymphoid organs[3]. These nutritional changes do not all cause weight loss. (Pre)oedema, water and sodium retention, and hepatomegaly rather act in the opposite direction. Yet, because muscle wasting usually is the most important component, the net result is mostly weight loss, except in some very acute forms of kwashiorkor. The components of nutritional weight change have a different timing. Also, a same weight (for age or for height) or a same weight loss may represent different degrees of severity. For example, the same weight loss is more severe if there is pre-oedema and/or hepatomegaly. Single body weight measurements cannot distinguish whether or not a patient is in negative nitrogen balance. For example, many stunted (low height-for-age) children also have a very low WFA but are no longer acutely malnourished. They are anabolic again; this dramatically improves their prognosis compared to their former status[4]. Some low birth weight infants may have been malnourished *in utero* only and have high weight velocity but low WFA. It should thus be clear that there is no straightforward relationship between WFA, WFH or weight velocity and severity of PEM. The use of WFA or WFH reference cut-offs[1,17] is inappropriate not only for assessing the severity of malnutrition but even for determining the presence or absence of malnutrition. Indeed, it has been shown that children with a WFA or WFH falling within the so-called normal limits may be clinically malnourished, even severely marasmic[18]. It appears that such normal-weight malnutrition, also called clinical-anthropometrical mismatch, is probably very frequent. The reason might be that children who are genetically predisposed to grow along higher percentile lines, may, as a result of undernutrition, drop to lower, still 'normal', percentiles but become clinically malnourished. On the other hand, some children below the reference may just be genetically small and light.

ACCURACY OF PREDICTION

In spite of the inappropriateness of weight-based anthropometric indicators for individual nutritional diagnosis, on the population level, prevalence and severity of PEM increase with lower anthropometric scores. This explains why epidemiologic studies have found that child mortality increases with lowering WFA or WFH or weight velocity[19,20,21]. The form of the relationship seems to be (double) exponential[15]. According to Pelletier and co-workers, the relationship is of a log-linear type[22], which they regard as indicating a multiplicative rather than an additive interaction between disease exposure and malnutrition in the causation of mortality. Because of the existence of an epidemiologic relationship between mortality and weight-based anthropometric indicators, these indicators have been used to predict mortality in individuals[4,21,23]. The predictive capacity of these methods is disappointingly low, however. This is not only because of the lack of straightforward relationship between severity of PEM and the weight-based indicators, but also because death is usually a relatively rare event, even in areas with high mortality and even in malnourished children. In very ill, severely malnourished hospitalized children, the accuracy of prediction seems to be better[1]. Weight-based anthropometric indices have also been used for delineating high-risk subgroups of children for selective nutritional rehabilitation measures. Such selection methods should be regarded as inappropriate. 'Underweight' (low WFA) and 'wasted' (low WFH) children are only a fraction of all malnourished children. Even severely marasmic children may not be detected by these methods. To direct nutritional interventions selectively to 'underweight' or 'wasted' children may indeed help a subgroup of children with an increased risk of death, but will not much influence the prevalence of malnutrition and mortality in the community.

CAUSE OF DEATH

It is difficult to quantify the contribution of PEM to the high rates of death in early childhood in deprived areas. One problem is that most cause-specific mortality statistics usually do not indicate nutritional deficiencies as a cause of death. There are severe diagnostic problems both with anthropometry and with 'verbal autopsies' and it is difficult to discern primary and contributory causes of death. In mortality statistics, infections, especially diarrhoea and acute respiratory infections are mostly mentioned as primary causes. Infections and malnutrition may increase each other's severity but have also properties that may lead independently to a fatal outcome. So far, it is not clear how much mild to moderate malnutrition may contribute but that contribution is probably high[18,22,24,25]. The contribution of malnutrition to mortality in a particular area varies not only with its prevalence and severity, but also with prevailing pattern of diseases[26]. Malaria is considered to be unrelated to nutritional status whereas malnutrition and diarrhoea are almost inseparable. Hence, in areas with malaria hyperendemicity and low prevalence of diarrhoea, the contribution of malnutrition to mortality is expected to be lower for the same prevalence of malnutrition[27]. Thus, it is clear that accurate estimation of the contribution of malnutrition to child mortality becomes very complicated if not impossible. For practical comparative purposes, however, it has become common practice to base these estimations either on prevalences of 'wasting', 'underweight'[25], or on the risks of death associated with them.

CONCLUSION

To conclude, the relationship between malnutrition and mortality is complex, difficult to study and not fully understood. Malnutrition is a symptom of poverty, at least in the majority of the Third World children. For them, nutritional interventions in their many forms can not be but a symptomatic treatment of one of the many effects of poverty on populations. Poverty itself is not just monetary. It is political, affecting the fabric of society, cultural and social, affecting the status of women and children, and also has educational input, depriving parents of the knowledge they need to care for their children. Indeed, health should be a sustainable state[28] but global poverty and one of its correlates, malnutrition, are all too often self-sustaining states. This remains a painful truth after several decades of development aid projects in the Third World. The many mechanisms by which this state is sustained and the ways they could be countered are just beginning to be understood. Thus, there is some hope that the inclusion of measures which produced sustained change into integrated development programmes, will eventually lead to greater and durable reductions of malnutrition and mortality.

REFERENCES

1 Gomez F, Galvan RR, Frenk S, Munoz JC, Chavez R, Vazques J. Mortality in second and third degree malnutrition. *J Trop Pediatr* 1956;**2**:277–83

2 Baker JP, Detsky AS, Wesson DE, Wolman SL, Stewart S, Whitewell J, *et al.* Nutritional assessment. A comparison of clinical judgement and objective measurements. *N Engl J Med* 1982;**306**:969–72

3 Keusch GT. Malnutrition, infection, and immune function. In: Suskind RM, Lewinter-Suskind L, eds. *The Malnourished Child.* Nestlé Nutrition Workshop Series, Vol 19. New York: Vevey/Raven Press, 1990

4 Briend A, Dykewicz C, Graven K, Mazumder RN, Wojtiniak B, Bennish M. Usefulness of nutritional indices and classifications in predicting death of malnourished children. *BMJ* 1986;**293**:373–5

5 Briend A, Garenne M, Maire B, Fontaine O, Dieng K. Nutritional status, age and survival: the muscle mass hypothesis. *Eur J Clin Nutr* 1989;**43**:715–26

6 Lackritz EM, Campbell CC, Ruebush TK, *et al.* Effect of blood transfusion on survival among children in a Kenyan hospital. *Lancet* 1992;**340**:524–8

7 Golden BE. Primary protein-energy malnutrition. In: Garrow JS, James WPT, eds. *Human Nutrition and Dietetics.* Edinburgh: Churchill Livingstone, 1993

8 Talner NS. Cardiac changes in the malnourished Child. In: Suskind M, Lewinter-Suskind L eds. The *Malnourished Child.* Nestlé Workshop Series, Vol. 19. New York: Vevey/Raven Press; 1990

9 Ballabriga A. Protein-energy malnutrition. In: Buts JP, Sokal EM, eds. *Management of Digestive and Liver Disorders in Infants and Children.* Buts JP, Sokal EM, eds. Amsterdam: Elsevier Science Publishers, 1993:223–49

10 Gillam SJ. Mortality risk factors in acute protein-energy malnutrition. *Trop Doct* 1989;**19**:82–5

11 Sandberg L, Owens AJ, VanReken D, Horowitz B, Fredell JE, Takyi Y, *et al.* Improvement in plasma protein concentrations with fibronectin treatment in severe malnutrition. *Am J Clin Nutr* 1990;**52**:651–6

12 Ghana VAST Study Team. Vitamin A supplementation in northern Ghana: effects on clinic attendances, hospital admissions, and child mortality. *Lancet* 1993;**342**:7–12

13 Chahnazarian A, Ewbank DC, Makani B, Ekouevi K. Impact of selective primary care on childhood mortality in a rural health zone of Zaire. *Int J Epidemiol* 1993;**22**:S32–S41

14 Bhuiya A, Wojtyniak B, Karim R. Malnutrition and child mortality: are socio-economic factors important? *J Biosoc Sci* 1989;**21**:357–64

15 Fauveau V, Briend A, Chakraborty J, Sarder AM. The contribution of severe malnutrition to child mortality in rural Bangladesh: implications for targeting nutritional intervention. *Food Nutr Bull* 1990;**12**:215–19

16 Van den Broeck J, Eeckels R. Effect of malnutrition on child mortality. *Lancet* 1994;**344**:273

17 Waterlow JC. Some aspects of childhood malnutrition as a public health problem. *BMJ* 1974;**4**:88–90

18 Van den Broeck J, Meulemans W, Eeckels R. Nutritional assessment: the problem of clinical-anthropometrical mismatch. *Eur J Clin Nutr* 1994;**48**:60–5

19 Vella V, Tomkins A, Ndiku J, Marshal T, Cortinovis I. Anthropometry as a predictor for mortality among Ugandan children, allowing for socio-economic variables. *Eur J Clin Nutr* 1994;**48**:189–97

20 Chen LC, Chowdhury A, Huffman SL. Anthropometric assessment of energy-protein malnutrition and subsequent risk of mortality among preschool aged children. *Am J Clin Nutr* 1980;**33**:1836–45

21 Van Lerberghe W. *Kasongo: Child Mortality and Growth in a small African Town.* London: Smith-Gordon, 1990:1–159

22 Pelletier DL, Frongillo EA, Habicht JP. Epidemiologic evidence for a potentiating effect of malnutrition on child mortality. *Am J Public Health* 1993;**83**:1130–33

23 Briend A, Bari A. Critical assessment of the use of growth monitoring for identifying children with a high risk of dying in primary health care programmes. *BMJ* 1989;**298**:1607–11

24 Booth IW. Costing malnutrition: add or multiply? *Lancet* 1994;**343**:554–5

25 World Bank. *World Development Report 1993.* Oxford: Oxford University Press, 1993

26 Waterlow JC. Malnutrition and mortality. In: Waterlow JC, ed. *Protein Energy Malnutrition.* London: Edward Arnold, 1992:324–39

27 Van den Broeck J, Eeckels R, Vuylsteke J. Influence of nutritional status on child mortality in rural Zaire. *Lancet* 1993;**341**:1491–5

28 King M. Health is a sustainable state. *Lancet* 1990;**336**:664–7

(Accepted 7 December 1994)